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NEWS 8	FEB 16	INSPEC Adding Its Own IPC codes and Author's E-mail Addresses
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NEWS 11	APR 02	DWPI: New display format ALLSTR available
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NEWS 14	APR 07	CA/CAplus CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
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NEWS 16	APR 07	MEDLINE Coverage Is Extended Back to 1947
NEWS 17	JUN 16	WPI First View (File WPIFV) will no longer be available after July 30, 2010
NEWS 18	JUN 18	DWPI: New coverage - French Granted Patents
NEWS 19	JUN 18	CAS and FIZ Karlsruhe announce plans for a new STN platform
NEWS 20	JUN 18	IPC codes have been added to the INSPEC backfile (1969-2009)
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NEWS 22	JUN 21	Access an additional 1.8 million records exclusively enhanced with 1.9 million CAS Registry Numbers -- EMBASE Classic on STN
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                                                        ENTRY    SESSION
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FILE 'MEDLINE' ENTERED AT 14:57:00 ON 28 JUN 2010

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=> s Sayers J?/AU
L1          385 SAYERS J?/AU

=> s l1 and growth(w)hormone
L2           22 L1 AND GROWTH(W) HORMONE

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           19 DUP REM L2 (3 DUPLICATES REMOVED)

=> s ARTYMIUK P?/AU
L4          363 ARTYMIUK P?/AU

=> s l4 and growth(w)hormone
L5           19 L4 AND GROWTH(W) HORMONE

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6           16 DUP REM L5 (3 DUPLICATES REMOVED)

=> s ROSS R?/AU
L7        11282 ROSS R?/AU

=> s l7 and growth(w)hormone
L8          365 L7 AND GROWTH(W) HORMONE
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=> s 18 and ligand
L9          28 L8 AND LIGAND

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10          16 DUP REM L9 (12 DUPLICATES REMOVED)

=> dis his

     (FILE 'HOME' ENTERED AT 14:56:38 ON 28 JUN 2010)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:57:00 ON 28 JUN 2010
L1          385 S SAYERS J?/AU
L2           22 S L1 AND GROWTH(W)HORMONE
L3           19 DUP REM L2 (3 DUPLICATES REMOVED)
L4          363 S ARTYMIUK P?/AU
L5           19 S L4 AND GROWTH(W)HORMONE
L6           16 DUP REM L5 (3 DUPLICATES REMOVED)
L7        11282 S ROSS R?/AU
L8          365 S L7 AND GROWTH(W)HORMONE
L9           28 S L8 AND LIGAND
L10          16 DUP REM L9 (12 DUPLICATES REMOVED)

=> dis ibib abs l3 1-19

L3   ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:         2010:238593  CAPLUS
DOCUMENT NUMBER:          152:304118
TITLE:                    Glucagon-like peptide I (GLP-1) fusions with
                          GLP-1-binding proteins, such as dipeptidyl peptidase
                          IV (DDP4), and antidiabetic uses thereof
INVENTOR(S):              Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S):       Asterion Ltd., UK
SOURCE:                   PCT Int. Appl., 72pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     --------------      ----   --------    --------------------    --------
     WO 2010020767        A2    20100225    WO 2009-GB2006          20090818
          W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
              CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG,
              ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP,
              KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,
              MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE,
              PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV,
              SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
          RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
              IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI,
              SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
              SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,
              ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                        GB 2008-15248       A  20080821
                                              US 2008-90813P      P  20080821
                                              GB 2009-7794        A  20090507
                                              GB 2009-13901       A  20090810
OTHER SOURCE(S):          MARPAT 152:304118
```

AB The inventors describe nucleic acid mols. that encode fusion polypeptides comprising GLP-1 (glucagon-like peptide I), or a receptor binding part thereof, linked directly or indirectly to a polypeptide that naturally binds GLP-1. In one embodiment GLP-1 is linked to an extracellular domain of a glucagon-like peptide-1 receptor (GLP-1 receptor, GLP1R). Alternative embodiments include the fusion of GLP-1 to inactivated dipeptidyl peptidase IV (DDP4, CD26) and optionally inactive adenosine deaminase (ADA), such as in the provided GLP1/DPP4/ADA fusion protein 10G1.

L3 ANSWER 2 OF 19 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2009:333182 BIOSIS
DOCUMENT NUMBER: PREV200900334285
TITLE: Modified growth hormone fusion polypeptides.
AUTHOR(S): Ross, Richard [Inventor]; Anonymous; Sayers, Jon [Inventor]; Artymiuk, Peter [Inventor]
CORPORATE SOURCE: Sheffield, United Kingdom
ASSIGNEE: Asterion Limited
PATENT INFORMATION: US 07524649 20090428
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (APR 28 2009)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 27 May 2009
Last Updated on STN: 27 May 2009
AB The invention relates to chimeric polypeptides wherein said polypeptides comprise a modified binding domain of growth hormone linked to a receptor binding domain of growth hormone receptor; and tandems/oligomers of said modified growth hormone binding domains.

L3 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2009:1048978 CAPLUS
DOCUMENT NUMBER: 151:307229
TITLE: Linker peptides including glycosylation sites for use in fusion proteins
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 185pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009103965	A1	20090827	WO 2009-GB437	20090218

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,

ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: GB 2008-2978 A 20080219
GB 2008-21076 A 20081119
GB 2009-539 A 20090114
OTHER SOURCE(S): MARPAT 151:307229
AB Peptide linkers that contain a glycosylation site and that can be used in the manufacture of fusion proteins that interact with membranes, e.g. fusion proteins of proteins and their cognate receptors. Glycosylation site motif variants for use in linker peptides are described.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2009:791326 CAPLUS
DOCUMENT NUMBER: 151:132011
TITLE: Peptide fusion proteins for cancer therapy
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009081170	A2	20090702	WO 2008-GB4279	20081224
WO 2009081170	A3	20091203		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: GB 2007-25201 A 20071224
AB We disclose fusion proteins comprising a peptide comprising a binding domain for a receptor which is linked to a polypeptide comprising the binding domain to which said peptide binds.

L3 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2009:457596 CAPLUS
DOCUMENT NUMBER: 150:391157
TITLE: Protein and nucleotide sequences of modified growth hormone polypeptides
INVENTOR(S): Artymiuk, Peter; Ross, Richard A.; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2009047474	A2	20090416	WO 2008-GB3056		20080910
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2008309386	A1	20090416	AU 2008-309386		20080910
KR 2010067686	A	20100621	KR 2010-710215		20080910
PRIORITY APPLN. INFO.:			US 2007-979010P	P	20071010
			GB 2007-19818	A	20071011
			WO 2008-GB3056	W	20080910

AB The invention relates to modified growth hormone fusion proteins and dimers comprising said fusion proteins; nucleic acid mols. encoding said proteins and methods of treatment that use said proteins in the treatment of conditions that result from growth hormone excess. The protein and nucleotide sequences of modified growth hormone fusion protein for treatment of growth hormone related diseases.

L3 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER:	2009:177456 CAPLUS
DOCUMENT NUMBER:	150:206809
TITLE:	Insulin-like growth factor fusion proteins and therapeutic uses thereof
INVENTOR(S):	Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S):	Asterion Limited, UK
SOURCE:	PCT Int. Appl., 47pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

WO 2009019465	A1	20090212	WO 2008-GB2655		20080805
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2190874	A1	20100602	EP 2008-776130		20080805
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS					
IN 2010KN00777	A	20100521	IN 2010-KN777		20100301

PRIORITY APPLN. INFO.: GB 2007-15213 A 20070806
US 2007-956333P P 20070816
WO 2008-GB2655 W 20080805

AB This disclosure relates to insulin-like growth factor fusion polypeptides and nucleic acid mols. encoding said polypeptides. The fusion polypeptide comprises insulin-like growth factor, or active part thereof linked, directly or indirectly, to at least one insulin-like growth factor-binding domain of the insulin-like growth factor receptor. The invention also relates to methods of treating insulin-like growth factor deficiency related disorders with said polypeptides and nucleic acid mols. A method for preparing a hybridoma cell-line producing monoclonal antibodies which bind said polypeptides is also presented.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2009:115655 CAPLUS
DOCUMENT NUMBER: 150:161106
TITLE: Growth hormone fusion proteins
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009013461	A1	20090129	WO 2008-GB2406	20080716
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2008278907	A1	20090129	AU 2008-278907	20080716
CA 2693951	A1	20090129	CA 2008-2693951	20080716
EP 2170943	A1	20100407	EP 2008-775945	20080716
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
KR 2010043201	A	20100428	KR 2010-702192	20080716
CN 101679504	A	20100324	CN 2008-80021473	20091222

PRIORITY APPLN. INFO.: US 2007-951122P A 20070720
GB 2007-17985 A 20070914
WO 2008-GB2406 W 20080716

AB We disclose growth hormone fusion proteins that have increased in vivo stability and activity; nucleic acid mols. encoding said proteins and methods of treatment of growth hormone deficiency that use said proteins. This disclosure relates to the biol. actions of a ligand-receptor fusion (LR-fusion) of GH with its extracellular domain receptor. Such a genetically engineered LR-fusion protein was purified from mammalian cell culture. In rats the LR-fusion

had a 300-times reduced clearance compared to native GH and single administration promoted growth for 10 days far superior to that seen with native GH. The reduced clearance is reproducible in a primate model. The LR-fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone as occurs naturally with GH and its binding protein. A recombinant gene encoding human GH linked to the A & B domains of the GHR extracellular domain (exGHR1-238) via a flexible (Gly4Ser)4 linker, was generated (Fig. 1 c).
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 19 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2009:137246 BIOSIS
DOCUMENT NUMBER: PREV200900137246
TITLE: Fusion protein comprising growth hormone and growth hormone receptor.
AUTHOR(S): Ross, Richard [Inventor]; Anonymous; Artymiuk, Peter [Inventor]; Sayers, Jon [Inventor]
CORPORATE SOURCE: Sheffield, United Kingdom
ASSIGNEE: Asterion Limited
PATENT INFORMATION: US 07446183 20081104
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (NOV 4 2008)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Feb 2009
Last Updated on STN: 18 Feb 2009
AB This invention relates to agents which bind to cell surface receptors; methods to manufacture said agents; therapeutic compositions comprising said agents; and screening methods to identify novel agents.

L3 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2008:352889 CAPLUS
DOCUMENT NUMBER: 148:347917
TITLE: Growth factor chimeric protein for use in non-human animals
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008032059	A2	20080320	WO 2007-GB3453	20070913
WO 2008032059	A3	20080508		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20090270325	A1	20091029	US 2009-441361		20090319
PRIORITY APPLN. INFO.:			GB 2006-18082	A	20060914
			WO 2007-GB3453	W	20070913

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB We describe a chimeric protein comprising a growth hormone polypeptide linked to a polypeptide comprising the extracellular binding domain of growth hormone receptor; its use in enhancing the growth and metabolism of non-human animals and homodimers comprising said chimeric protein.

L3 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER:	2007:1303035 CAPLUS
DOCUMENT NUMBER:	147:535195
TITLE:	Fusion protein composed of circularly permuted growth hormone antagonist GHCP07C, extracellular domain of receptor, and human modified prolactin, and its use in construction of pharmaceutical compositions for treating disorders
INVENTOR(S):	Pradhananga, Sarbendra; Sayers, John; Ross, Richard; Artymiuk, Peter
PATENT ASSIGNEE(S):	Asterion Limited, UK
SOURCE:	PCT Int. Appl., 46pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007128979	A1	20071115	WO 2007-GB1285	20070405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007246913	A1	20071115	AU 2007-246913	20070405
CA 2648487	A1	20071115	CA 2007-2648487	20070405
EP 2004681	A1	20081224	EP 2007-732329	20070405
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2009532051	T	20090910	JP 2009-503658	20070405
CN 101389649	A	20090318	CN 2007-80006944	20080827
KR 2008109814	A	20081217	KR 2008-724266	20081002
MX 2008012934	A	20081015	MX 2008-12934	20081006
IN 2008KN04414	A	20090306	IN 2008-KN4414	20081103
US 20100035804	A1	20100211	US 2009-296180	20090616
PRIORITY APPLN. INFO.:			GB 2006-6946	A 20060406
			WO 2007-GB1285	W 20070405

AB The invention provides nucleic acid mols. encoding the circularly permuted human growth hormone GHCP07 and variants thereof, wherein variants contain amino acid changes at the receptor binding sites and acts as growth hormone receptor antagonists. The

invention also provides the amino acid sequences of GHCP07, and antagonist GHCP07C, wherein GHCP07C contains a C-terminal region of human growth hormone (GH) linked to a N-terminal region of GH, with a changes in amino acids at receptor binding sites, such as Glycine to Arginine at position 176. The invention further provides various fusion proteins comprised of: (a) at least two GHCP07C polypeptides linked in tandem; (b) extracellular binding domains of growth hormone receptor (GHR) linked to at least two GHCP07 polypeptides; (c) GHCP07C polypeptides linked to a human prolactin modified polypeptide (such as G129R PRL); and/or (d) GHCP07C-human modified prolactin fusions containing an extracellular domain of receptors, such as cytokine, GH, prolactin receptors. The invention was based on the general knowledge that the G129R mutation in PRL and G120R mutation in GH disrupt the structural integrity of the two receptor sites, and results in proteins acting as receptor antagonists. Still further, the invention provides: (a) nucleic acid mols. encoding the disclosed fusion proteins and their use in construction of vectors for recombinant protein production; and (b) the amino acid sequences of said extracellilar domains found in human GHR and the modified human prolactin (G129R). Finally, the invention provides for the use of the disclosed antagonists, and/or their fusion proteins, and/or their nucleic acids in construction of a pharmaceutical compn which can be use to treat various conditions, such as gigantism, acromegaly, cancer, diabetic retinopathy, diabetic nephropathy and/or other complications of diabetes and/or GH excess. In the examples, the invention presented mol. genetics methods used to generate circularly permutated growth hormone antagonists GHCP07BHis and GHCP07C, and showed that both proteins had antagonistic activity.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 19 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2007527470 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17721547
TITLE: A ligand-receptor fusion of growth hormone forms a dimer and is a potent long-acting agonist.
AUTHOR: Wilkinson Ian R; Ferrandis Eric; Artymiuk Peter J; Teillot Marc; Soulard Chantal; Touvay Caroline; Pradhananga Sarbendra L; Justice Sue; Wu Zida; Leung Kin C; Strasburger Christian J; Sayers Jon R; Ross Richard J
CORPORATE SOURCE: School of Medicine and Biomedical Sciences, Royal Hallamshire Hospital, University of Sheffield, Sheffield S10 2JF, UK.
SOURCE: Nature medicine, (2007 Sep) Vol. 13, No. 9, pp. 1108-13. Electronic Publication: 2007-08-26. Journal code: 9502015. ISSN: 1078-8956. L-ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200803
ENTRY DATE: Entered STN: 11 Sep 2007 Last Updated on STN: 13 Mar 2008 Entered Medline: 12 Mar 2008

AB Cytokine hormones have a short plasma half-life and require frequent administration. For example, growth hormone replacement involves daily injections. In common with other cytokines, the extracellular domain of the growth hormone

receptor circulates as a binding protein, which naturally prolongs the biological half-life of growth hormone. Here we have studied the biological actions of a ligand-receptor fusion of growth hormone and the extracellular domain of its receptor. The genetically engineered ligand-receptor fusion protein was purified from mammalian cell culture. In rats, the ligand-receptor fusion had a 300-times reduced clearance as compared to native growth hormone, and a single injection promoted growth for 10 d, far exceeding the growth seen after administration of native growth hormone. The ligand-receptor fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone similar to the natural reservoir of growth hormone and its binding protein. In conclusion, a ligand-receptor fusion of cytokine to its extracellular receptor generates a potent, long-acting agonist with exceptionally slow absorption and elimination. This approach could be easily applied to other cytokines.

L3 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:104499 CAPLUS
DOCUMENT NUMBER: 144:219144
TITLE: Recombinant dimers of cytokine receptor-binding domains linked by inflexible helical linkers for modulation of cytokine signaling
INVENTOR(S): Artymiuk, Peter; Pradhananga, Sarbendra; Sayers, John; Ross, Richard
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010891	A2	20060202	WO 2005-GB2826	20050718
WO 2006010891	A9	20060427		
WO 2006010891	A3	20060608		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SZ, BE, CY, FR, GR, IE, IT, MC, NL, SI, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2005266184	A1	20060202	AU 2005-266184	20050718
CA 2575441	A1	20060202	CA 2005-2575441	20050718
EP 1771467	A2	20070411	EP 2005-761593	20050718
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101014616	A	20070808	CN 2005-80030121	20050718
JP 2008507292	T	20080313	JP 2007-523141	20050718
NZ 553224	A	20090531	NZ 2005-553224	20050718
RU 2391353	C2	20100610	RU 2007-106043	20050718
MX 2007001180	A	20070413	MX 2007-1180	20070126

KR 2007067678	A	20070628	KR 2007-703976		20070220
KR 891509	B1	20090406			
IN 2007KN00631	A	20070706	IN 2007-KN631		20070221
KR 2009006221	A	20090114	KR 2008-729058		20081127
US 20090221477	A1	20090903	US 2009-658526		20090416
PRIORITY APPLN. INFO.:			US 2004-591358P	P	20040726
			GB 2004-16687	A	20040727
			GB 2005-2839	A	20050211
			WO 2005-GB2826	W	20050718
			KR 2007-703976	A3	20070220

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB We disclose therapeutic proteins comprising at least two domains capable of binding to a cytokine receptor, wherein the domains are connected by a peptide linker, wherein the linker optionally comprises a rigid alpha helical region. These proteins may act as agonists or antagonists of cytokine signaling. Thus, growth hormone receptor-binding growth hormone fragments were dimerized using a rigid or semi-rigid linker. The rigid linker comprised the motif A(EAAAK)nA, with n = 1-5 preferred. These proteins were produced with transgenic E. coli. The growth hormone activity of these proteins was equal to or greater than growth hormone itself.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:34776 CAPLUS

DOCUMENT NUMBER: 142:127937

TITLE: Modified cytokine ligand polypeptides preparation, screening, and uses thereof for treatment

INVENTOR(S): Sayers, Jon; Artymuik, Peter; Ross, Richard

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003165	A2	20050113	WO 2004-GB2827	20040628
WO 2005003165	A3	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2568859	A1	20050113	CA 2004-2568859	20040628
EP 1639002	A2	20060329	EP 2004-743175	20040628
EP 1639002	B1	20100505		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

JP 2008504001	T	20080214	JP 2006-518330		20040628
AT 466880	T	20100515	AT 2004-743175		20040628
US 20070264234	A1	20071115	US 2007-561831		20070316
PRIORITY APPLN. INFO.:			GB 2003-15182	A	20030628
			WO 2004-GB2827	W	20040628

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The disclosed invention describes modified cytokine ligand polypeptides comprising a modified amino acid sequence which is a modification of the native cytokine amino acid sequence of said ligand, wherein the native N terminal and C terminal amino acid residues of the native polypeptide are linked, directly or indirectly, together, characterized in that said ligand is provided with alternative N terminal and C terminal amino acid residues and further wherein at least one binding domain for said ligand's cognate binding partner or receptor complex is disrupted. The authors describe the first embodiment of the growth hormone circular permutation GH CP01, with the N terminus Ile121 and the C terminus Glu118. The "old" termini of GH were linked by a 6 amino acid linker, formed by joining the "old" termini -3 amino acids from the first helix at the N terminus and +3 residues for the last helix at the C terminus. E. coli cells were used as the expression system. Also described are alternative approaches to construct circular permutations of GH.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:878488 CAPLUS

DOCUMENT NUMBER: 141:344597

TITLE: Chimeric proteins containing cytokine receptor binding domain and glycosylphosphatidylinositol anchor and their therapeutic uses

INVENTOR(S): Ross, Richard; Sayers, Jon; Artymiuk, Peter

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004090135	A2	20041021	WO 2004-GB1572	20040407
WO 2004090135	A3	20050428		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1616010	A2	20060118	EP 2004-726219	20040407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007527695	T	20071004	JP 2006-506114	20040407

US 20060205926	A1	20060914	US 2005-552388	20051007
US 7625998	B2	20091201		

PRIORITY APPLN. INFO.:

GB 2003-8088	A	20030409
GB 2003-24235	A	20031016
WO 2004-GB1572	W	20040407

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to polypeptides which comprise a ligand-binding domain of a cytokine receptor fused with a signal sequence for the attachment of glycosylphosphatidylinositol (GPI) anchors. GPI-anchors are post-translational modifications to proteins that add glycosylphosphatidylinositol which enable these proteins to anchor to the extracellular side of cell membranes. 1B1-GP1 was constructed, in which GH was linked through its C-terminus to the extracellular domain of the GH receptor and then linked to the GPI signal sequence. 1C1-GPI was also constructed, in which a tandem of GH was linked through the second GH C-terminus to the GPI signal sequence. The invention provides vectors and CHO-K1 cells for expressing GHBP-GPI.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 19 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:225928 BIOSIS
DOCUMENT NUMBER: PREV200400225966
TITLE: Tandem fusions of growth hormone and its G120R mutated antagonist retain biological activity and demonstrate prolonged plasma half-life.
AUTHOR(S): Pradhananga, S. L. [Reprint Author]; Wilkinson, I. [Reprint Author]; Haylor, J. [Reprint Author]; Rezaee, S. [Reprint Author]; Artymiuk, P.; Sayers, J.; Ross, R. J. M. [Reprint Author]
CORPORATE SOURCE: Department of Clinical Sciences, Sheffield University, Sheffield, UK
SOURCE: Growth Hormone & IGF Research, (April 2004) Vol. 14, No. 2, pp. 116. print.
Meeting Info.: Second International GH-IGF Symposium. Queensland, Australia. April 18-22, 2004.
ISSN: 1096-6374 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Apr 2004
Last Updated on STN: 21 Apr 2004

L3 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:591215 CAPLUS
DOCUMENT NUMBER: 139:144956
TITLE: Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in therapy
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003062276	A2	20030731	WO 2003-GB253	20030124
WO 2003062276	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2510751	A1	20030731	CA 2003-2510751	20030124
EP 1468020	A2	20041020	EP 2003-702702	20030124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005529583	T	20051006	JP 2003-562153	20030124
RU 2325400	C2	20080527	RU 2004-121969	20030124
MX 2004007160	A	20050331	MX 2004-7160	20040723
BR 2004003173	A	20060321	BR 2004-3173	20040730
US 20050214762	A1	20050929	US 2005-502344	20050511
PRIORITY APPLN. INFO.:			GB 2002-1679 A	20020125
			WO 2003-GB253 W	20030124

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to the provision of oligomeric polypeptides (dimers, trimers, etc) comprising the ligand binding domains of cytokines which are linked via flexible polypeptide linker mols. The linker mols. optionally comprise protease sensitive sites to modulate the release of biol. active cytokines when administered to a human or animal subject. The invention also relates to chemical crosslinkers wherein the chemical crosslinkers serve to link the ligand binding domains. The chimeric cytokine can be used for treating acromegaly, gigantism, GH deficiency, Turners syndrome, renal failure, osteoporosis, diabetes mellitus, cancer, obesity, insulin resistance, hyperlipidemia, hypertension, anemia, autoimmune and infectious disease, inflammatory disorders including rheumatoid arthritis.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:949911 CAPLUS

DOCUMENT NUMBER: 140:13709

TITLE: Polypeptide having a plurality of modified growth hormone receptor binding domains from growth hormone, and therapeutic use

INVENTOR(S): Ross, Richard; Sayers, Jon; Artymuik, Peter

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: Brit. UK Pat. Appl., 31 pp.
CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2389115	A	20031203	GB 2003-20479	20011214

GB 2389115	B	20050316			
GB 2384001	A	20030716	GB 2001-30052		20011214
GB 2384001	B	20040204			
AU 2008201889	A1	20080522	AU 2008-201889		20080430
PRIORITY APPLN. INFO.:			GB 2001-30052	A3	20011214
			AU 2002-366325	A3	20021206

AB A chimeric polypeptide having a first and a second modified growth hormone receptor binding domain from growth hormone wherein the modification may be a deletion, substitution or addition of at least one amino acid residue and the said binding domains are joined in tandem. The binding domain may be modified in one of either site 1 or site 2 or at both sites 1 and 2. Specific modifications of said sites are disclosed as are linkers, polynucleotides encoding said polypeptides, vectors, cells expressing said polypeptide and methods of expressing said polypeptides. Pharmaceutical compns. comprising said polypeptides and their uses in treating diseases such as giantism, acromegaly, cancer, diabetic retinopathy, nephropathy or complications are claimed. The polypeptide may have a plurality of modified binding domains, especially those modified at site 2.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:550165 CAPLUS
DOCUMENT NUMBER: 139:112729
TITLE: Chimeric growth hormone-growth hormone receptor proteins and therapeutic uses thereof
INVENTOR(S): Ross, Richard; Sayers, Jon; Artymuik, Peter
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: Brit. UK Pat. Appl., 46 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2384001	A	20030716	GB 2001-30052	20011214
GB 2384001	B	20040204		
GB 2389115	A	20031203	GB 2003-20479	20011214
GB 2389115	B	20050316		
CA 2468439	A1	20030828	CA 2002-2468439	20021206
WO 2003070765	A2	20030828	WO 2002-GB5523	20021206
WO 2003070765	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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AU 2002366325	A1	20030909	AU 2002-366325	20021206
AU 2002366325	B2	20080424		
EP 1456385	A2	20040915	EP 2002-806858	20021206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

HU	2004002496	A2	20050329	HU 2004-2496	20021206
CN	1604965	A	20050406	CN 2002-824781	20021206
CN	100558899	C	20091111		
JP	2005525106	T	20050825	JP 2003-569672	20021206
NZ	533550	A	20060224	NZ 2002-533550	20021206
NZ	543369	A	20070831	NZ 2002-543369	20021206
RU	2346047	C2	20090210	RU 2004-117777	20021206
CN	101638437	A	20100203	CN 2009-10164026	20021206
SG	160205	A1	20100429	SG 2007-5155	20021206
IN	2004KN00751	A	20060421	IN 2004-KN751	20040603
IN	227610	A1	20090116		
ZA	2004004488	A	20060329	ZA 2004-4488	20040607
MX	2004005675	A	20050419	MX 2004-5675	20040611
BR	2004003522	A	20060411	BR 2004-3522	20040825
US	20050123558	A1	20050609	US 2005-498497	20050114
US	7524649	B2	20090428		
ZA	2006000149	A	20061025	ZA 2006-149	20060106
KR	2006106862	A	20061012	KR 2006-716929	20060823
KR	848802	B1	20080728		
KR	2007108254	A	20071108	KR 2007-721636	20070920
KR	879553	B1	20090122		
IN	2008KN01333	A	20081226	IN 2008-KN1333	20080402
AU	2008201889	A1	20080522	AU 2008-201889	20080430
US	20090239801	A1	20090924	US 2009-389022	20090219
JP	2010043100	A	20100225	JP 2009-223065	20090928

PRIORITY APPLN. INFO.:	GB 2001-30052	A3	20011214
	AU 2002-366325	A3	20021206
	CN 2002-824781	A3	20021206
	JP 2003-569672	A3	20021206
	NZ 2002-533550	A3	20021206
	WO 2002-GB5523	W	20021206
	IN 2004-KN751	A3	20040603
	KR 2004-709055	A3	20040611
	US 2005-498497	A3	20050114
	KR 2006-716929	A3	20060823

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A chimeric polypeptide comprising at least one modified binding domain of growth hormone (GH) and a ligand binding domain of growth hormone receptor (GHR) is claimed, wherein the modification is the addition, deletion or substitution of at least one amino acid. Said binding domain may be site 1 of growth hormone, site 2 of growth hormone or both sites of growth hormone. The binding domain of the growth hormone receptor may be the extracellular domain of GHR more preferably the C-terminal SD-100 domain. Nucleic acids encoding such polypeptides, expression vectors and cells expressing such vectors are also claimed. The use of such polypeptides in the preparation of pharmaceuticals and in the treatment of diseases including gigantism, acromegaly, cancer and diabetic conditions is also claimed. Alternatively claimed is a chimeric polypeptide comprising more than two modified growth hormone binding domains.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:924005 CAPLUS

DOCUMENT NUMBER: 136:49347

TITLE: Chimeric binding agent comprising cytokine, linker and cytokine receptor and uses in modulating receptor activity and therapy

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096565	A2	20011220	WO 2001-GB2645	20010618
WO 2001096565	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2447632	A1	20011220	CA 2001-2447632	20010618
EP 1290170	A2	20030312	EP 2001-940731	20010618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004503243	T	20040205	JP 2002-510682	20010618
US 20040071655	A1	20040415	US 2003-311473	20030718
US 7446183	B2	20081104		
US 20090054336	A1	20090226	US 2008-175582	20080718

PRIORITY APPLN. INFO.:

GB 2000-14765	A	20000616
GB 2001-5969	A	20010310
GB 2001-6487	A	20010316
WO 2001-GB2645	W	20010618
US 2003-311473	A1	20030718

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides a binding agent comprising a first part capable of binding a ligand binding domain of a receptor linked to a second part comprising a receptor binding domain wherein said binding agent modulates the activity of the receptor. The inventors link growth hormone (GH), through its C-terminal and a linker to the N-terminus of the SD100 domain of growth hormone receptor (GHR). By varying the length of the linker inventors define a mol. that has the flexibility to allow binding of GH through site 1 to full length receptor at the cell surface. The invention also relates to methods, vectors and host cells for production of said chimeric binding agent.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	84.76	84.98

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.75	-12.75

FILE 'STNGUIDE' ENTERED AT 15:01:53 ON 28 JUN 2010

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 25, 2010 (20100625/UP).

=> dis his

(FILE 'HOME' ENTERED AT 14:56:38 ON 28 JUN 2010)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:57:00 ON 28 JUN 2010
L1 385 S SAYERS J?/AU
L2 22 S L1 AND GROWTH(W)HORMONE
L3 19 DUP REM L2 (3 DUPLICATES REMOVED)
L4 363 S ARTYMIUK P?/AU
L5 19 S L4 AND GROWTH(W)HORMONE
L6 16 DUP REM L5 (3 DUPLICATES REMOVED)
L7 11282 S ROSS R?/AU
L8 365 S L7 AND GROWTH(W)HORMONE
L9 28 S L8 AND LIGAND
L10 16 DUP REM L9 (12 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 15:01:53 ON 28 JUN 2010

=> dis ibib abs l6 1-16
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS' - CONTINUE? (Y)/N:y

L6 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2010:238593 CAPLUS
DOCUMENT NUMBER: 152:304118
TITLE: Glucagon-like peptide I (GLP-1) fusions with GLP-1-binding proteins, such as dipeptidyl peptidase IV (DDP4), and antidiabetic uses thereof
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Ltd., UK
SOURCE: PCT Int. Appl., 72pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010020767	A2	20100225	WO 2009-GB2006	20090818
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: GB 2008-15248 A 20080821

	US 2008-90813P	P	20080821
	GB 2009-7794	A	20090507
	GB 2009-13901	A	20090810

OTHER SOURCE(S): MARPAT 152:304118

AB The inventors describe nucleic acid mols. that encode fusion polypeptides comprising GLP-1 (glucagon-like peptide I), or a receptor binding part thereof, linked directly or indirectly to a polypeptide that naturally binds GLP-1. In one embodiment GLP-1 is linked to an extracellular domain of a glucagon-like peptide-1 receptor (GLP-1 receptor, GLP1R). Alternative embodiments include the fusion of GLP-1 to inactivated dipeptidyl peptidase IV (DDP4, CD26) and optionally inactive adenosine deaminase (ADA), such as in the provided GLP1/DPP4/ADA fusion protein 10G1.

L6 ANSWER 2 OF 16 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

ACCESSION NUMBER: 2009:333182 BIOSIS
DOCUMENT NUMBER: PREV200900334285
TITLE: Modified growth hormone fusion polypeptides.
AUTHOR(S): Ross, Richard [Inventor]; Anonymous; Sayers, Jon [Inventor]; Artymiuk, Peter [Inventor]
CORPORATE SOURCE: Sheffield, United Kingdom
ASSIGNEE: Asterion Limited
PATENT INFORMATION: US 07524649 20090428
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (APR 28 2009)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 27 May 2009
Last Updated on STN: 27 May 2009

AB The invention relates to chimeric polypeptides wherein said polypeptides comprise a modified binding domain of growth hormone linked to a receptor binding domain of growth hormone receptor; and tandems/oligomers of said modified growth hormone binding domains.

L6 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1048978 CAPLUS
DOCUMENT NUMBER: 151:307229
TITLE: Linker peptides including glycosylation sites for use in fusion proteins
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 185pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009103965	A1	20090827	WO 2009-GB437	20090218

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2008-2978 A 20080219
GB 2008-21076 A 20081119
GB 2009-539 A 20090114

OTHER SOURCE(S): MARPAT 151:307229

AB Peptide linkers that contain a glycosylation site and that can be used in the manufacture of fusion proteins that interact with membranes, e.g. fusion proteins of proteins and their cognate receptors. Glycosylation site motif variants for use in linker peptides are described.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:791326 CAPLUS
DOCUMENT NUMBER: 151:132011
TITLE: Peptide fusion proteins for cancer therapy
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009081170	A2	20090702	WO 2008-GB4279	20081224
WO 2009081170	A3	20091203		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: GB 2007-25201 A 20071224

AB We disclose fusion proteins comprising a peptide comprising a binding domain for a receptor which is linked to a polypeptide comprising the binding domain to which said peptide binds.

L6 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:457596 CAPLUS
DOCUMENT NUMBER: 150:391157
TITLE: Protein and nucleotide sequences of modified growth hormone polypeptides
INVENTOR(S): Artymiuk, Peter; Ross, Richard A.; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009047474	A2	20090416	WO 2008-GB3056	20080910
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2008309386	A1	20090416	AU 2008-309386	20080910
KR 2010067686	A	20100621	KR 2010-710215	20080910
PRIORITY APPLN. INFO.:			US 2007-979010P	P 20071010
			GB 2007-19818	A 20071011
			WO 2008-GB3056	W 20080910

AB The invention relates to modified growth hormone fusion proteins and dimers comprising said fusion proteins; nucleic acid mols. encoding said proteins and methods of treatment that use said proteins in the treatment of conditions that result from growth hormone excess. The protein and nucleotide sequences of modified growth hormone fusion protein for treatment of growth hormone related diseases.

L6 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2009:177456 CAPLUS
DOCUMENT NUMBER: 150:206809
TITLE: Insulin-like growth factor fusion proteins and therapeutic uses thereof
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009019465	A1	20090212	WO 2008-GB2655	20080805
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

EP 2190874 A1 20100602 EP 2008-776130 20080805
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS
IN 2010KN00777 A 20100521 IN 2010-KN777 20100301
PRIORITY APPLN. INFO.: GB 2007-15213 A 20070806
US 2007-956333P P 20070816
WO 2008-GB2655 W 20080805

AB This disclosure relates to insulin-like growth factor fusion polypeptides and nucleic acid mols. encoding said polypeptides. The fusion polypeptide comprises insulin-like growth factor, or active part thereof linked, directly or indirectly, to at least one insulin-like growth factor-binding domain of the insulin-like growth factor receptor. The invention also relates to methods of treating insulin-like growth factor deficiency related disorders with said polypeptides and nucleic acid mols. A method for preparing a hybridoma cell-line producing monoclonal antibodies which bind said polypeptides is also presented.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2009:115655 CAPLUS
DOCUMENT NUMBER: 150:161106
TITLE: Growth hormone fusion proteins
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009013461	A1	20090129	WO 2008-GB2406	20080716
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2008278907	A1	20090129	AU 2008-278907	20080716
CA 2693951	A1	20090129	CA 2008-2693951	20080716
EP 2170943	A1	20100407	EP 2008-775945	20080716
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
KR 2010043201	A	20100428	KR 2010-702192	20080716
CN 101679504	A	20100324	CN 2008-80021473	20091222

PRIORITY APPLN. INFO.: US 2007-951122P A 20070720
GB 2007-17985 A 20070914
WO 2008-GB2406 W 20080716

AB We disclose growth hormone fusion proteins that have increased in vivo stability and activity; nucleic acid mols. encoding said

proteins and methods of treatment of growth hormone deficiency that use said proteins. This disclosure relates to the biol. actions of a ligand-receptor fusion (LR-fusion) of GH with its extracellular domain receptor. Such a genetically engineered LR-fusion protein was purified from mammalian cell culture. In rats the LR-fusion had a 300-times reduced clearance compared to native GH and single administration promoted growth for 10 days far superior to that seen with native GH. The reduced clearance is reproducible in a primate model. The LR-fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone as occurs naturally with GH and its binding protein. A recombinant gene encoding human GH linked to the A & B domains of the GHR extracellular domain (exGHR1-238) via a flexible (Gly4Ser)4 linker, was generated (Fig. 1 c).
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 16 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2009:137246 BIOSIS
DOCUMENT NUMBER: PREV200900137246
TITLE: Fusion protein comprising growth hormone and growth hormone receptor.
AUTHOR(S): Ross, Richard [Inventor]; Anonymous; Artymiuk, Peter [Inventor]; Sayers, Jon [Inventor]
CORPORATE SOURCE: Sheffield, United Kingdom
ASSIGNEE: Asterion Limited
PATENT INFORMATION: US 07446183 20081104
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (NOV 4 2008)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Feb 2009
Last Updated on STN: 18 Feb 2009
AB This invention relates to agents which bind to cell surface receptors; methods to manufacture said agents; therapeutic compositions comprising said agents; and screening methods to identify novel agents.

L6 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2008:352889 CAPLUS
DOCUMENT NUMBER: 148:347917
TITLE: Growth factor chimeric protein for use in non-human animals
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008032059	A2	20080320	WO 2007-GB3453	20070913
WO 2008032059	A3	20080508		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,

TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20090270325 A1 20091029 US 2009-441361 20090319
PRIORITY APPLN. INFO.: GB 2006-18082 A 20060914
WO 2007-GB3453 W 20070913

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB We describe a chimeric protein comprising a growth hormone polypeptide linked to a polypeptide comprising the extracellular binding domain of growth hormone receptor; its use in enhancing the growth and metabolism of non-human animals and homodimers comprising said chimeric protein.

L6 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2007:1303035 CAPLUS
DOCUMENT NUMBER: 147:535195
TITLE: Fusion protein composed of circularly permuted growth hormone antagonist GHCP07C, extracellular domain of receptor, and human modified prolactin, and its use in construction of pharmaceutical compositions for treating disorders
INVENTOR(S): Pradhananga, Sarbendra; Sayers, John; Ross, Richard; Artymiuk, Peter
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007128979	A1	20071115	WO 2007-GB1285	20070405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007246913	A1	20071115	AU 2007-246913	20070405
CA 2648487	A1	20071115	CA 2007-2648487	20070405
EP 2004681	A1	20081224	EP 2007-732329	20070405
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2009532051	T	20090910	JP 2009-503658	20070405
CN 101389649	A	20090318	CN 2007-80006944	20080827
KR 2008109814	A	20081217	KR 2008-724266	20081002
MX 2008012934	A	20081015	MX 2008-12934	20081006
IN 2008KN04414	A	20090306	IN 2008-KN4414	20081103
US 20100035804	A1	20100211	US 2009-296180	20090616
PRIORITY APPLN. INFO.:			GB 2006-6946 A	20060406

AB The invention provides nucleic acid mols. encoding the circularly permuted human growth hormone GHCP07 and variants thereof, wherein variants contain amino acid changes at the receptor binding sites and acts as growth hormone receptor antagonists. The invention also provides the amino acid sequences of GHCP07, and antagonist GHCP07C, wherein GHCP07C contains a C-terminal region of human growth hormone (GH) linked to a N-terminal region of GH, with a changes in amino acids at receptor binding sites, such as Glycine to Arginine at position 176. The invention further provides various fusion proteins comprised of: (a) at least two GHCP07C polypeptides linked in tandem; (b) extracellular binding domains of growth hormone receptor (GHR) linked to at least two GHCP07 polypeptides; (c) GHCP07C polypeptides linked to a human prolactin modified polypeptide (such as G129R PRL); and/or (d) GHCP07C-human modified prolactin fusions containing an extracellular domain of receptors, such as cytokine, GH, prolactin receptors. The invention was based on the general knowledge that the G129R mutation in PRL and G120R mutation in GH disrupt the structural integrity of the two receptor sites, and results in proteins acting as receptor antagonists. Still further, the invention provides: (a) nucleic acid mols. encoding the disclosed fusion proteins and their use in construction of vectors for recombinant protein production; and (b) the amino acid sequences of said extracellilar domains found in human GHR and the modified human prolactin (G129R). Finally, the invention provides for the use of the disclosed antagonists, and/or their fusion proteins, and/or their nucleic acids in construction of a pharmaceutical compn which can be use to treat various conditions, such as gigantism, acromegaly, cancer, diabetic retinopathy, diabetic nephropathy and/or other complications of diabetes and/or GH excess. In the examples, the invention presented mol. genetics methods used to generate circularly permutated growth hormone antagonists GHCP07BHis and GHCP07C, and showed that both proteins had antagonistic activity.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2007527470 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17721547
TITLE: A ligand-receptor fusion of growth hormone forms a dimer and is a potent long-acting agonist.
AUTHOR: Wilkinson Ian R; Ferrandis Eric; Artymiuk Peter J ; Teillot Marc; Soulard Chantal; Touvay Caroline; Pradhananga Sarbendra L; Justice Sue; Wu Zida; Leung Kin C; Strasburger Christian J; Sayers Jon R; Ross Richard J
CORPORATE SOURCE: School of Medicine and Biomedical Sciences, Royal Hallamshire Hospital, University of Sheffield, Sheffield S10 2JF, UK.
SOURCE: Nature medicine, (2007 Sep) Vol. 13, No. 9, pp. 1108-13. Electronic Publication: 2007-08-26. Journal code: 9502015. ISSN: 1078-8956. L-ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200803
ENTRY DATE: Entered STN: 11 Sep 2007 Last Updated on STN: 13 Mar 2008

Entered Medline: 12 Mar 2008

AB Cytokine hormones have a short plasma half-life and require frequent administration. For example, growth hormone replacement involves daily injections. In common with other cytokines, the extracellular domain of the growth hormone receptor circulates as a binding protein, which naturally prolongs the biological half-life of growth hormone. Here we have studied the biological actions of a ligand-receptor fusion of growth hormone and the extracellular domain of its receptor. The genetically engineered ligand-receptor fusion protein was purified from mammalian cell culture. In rats, the ligand-receptor fusion had a 300-times reduced clearance as compared to native growth hormone, and a single injection promoted growth for 10 d, far exceeding the growth seen after administration of native growth hormone. The ligand-receptor fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone similar to the natural reservoir of growth hormone and its binding protein. In conclusion, a ligand-receptor fusion of cytokine to its extracellular receptor generates a potent, long-acting agonist with exceptionally slow absorption and elimination. This approach could be easily applied to other cytokines.

L6 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:104499 CAPLUS
DOCUMENT NUMBER: 144:219144
TITLE: Recombinant dimers of cytokine receptor-binding domains linked by inflexible helical linkers for modulation of cytokine signaling
INVENTOR(S): Artymiuk, Peter; Pradhananga, Sarbendra; Sayers, John; Ross, Richard
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010891	A2	20060202	WO 2005-GB2826	20050718
WO 2006010891	A9	20060427		
WO 2006010891	A3	20060608		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SZ, BE, CY, FR, GR, IE, IT, MC, NL, SI, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005266184	A1	20060202	AU 2005-266184	20050718
CA 2575441	A1	20060202	CA 2005-2575441	20050718
EP 1771467	A2	20070411	EP 2005-761593	20050718

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

CN 101014616	A	20070808	CN 2005-80030121		20050718
JP 2008507292	T	20080313	JP 2007-523141		20050718
NZ 553224	A	20090531	NZ 2005-553224		20050718
RU 2391353	C2	20100610	RU 2007-106043		20050718
MX 2007001180	A	20070413	MX 2007-1180		20070126
KR 20070076778	A	20070628	KR 2007-703976		20070220
KR 891509	B1	20090406			
IN 2007KN00631	A	20070706	IN 2007-KN631		20070221
KR 2009006221	A	20090114	KR 2008-729058		20081127
US 20090221477	A1	20090903	US 2009-658526		20090416
PRIORITY APPLN. INFO.:			US 2004-591358P	P	20040726
			GB 2004-16687	A	20040727
			GB 2005-2839	A	20050211
			WO 2005-GB2826	W	20050718
			KR 2007-703976	A3	20070220

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB We disclose therapeutic proteins comprising at least two domains capable of binding to a cytokine receptor, wherein the domains are connected by a peptide linker, wherein the linker optionally comprises a rigid alpha helical region. These proteins may act as agonists or antagonists of cytokine signaling. Thus, growth hormone receptor-binding growth hormone fragments were dimerized using a rigid or semi-rigid linker. The rigid linker comprised the motif A(EAAAK)nA, with n = 1-5 preferred. These proteins were produced with transgenic E. coli. The growth hormone activity of these proteins was equal to or greater than growth hormone itself.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:878488 CAPLUS

DOCUMENT NUMBER: 141:344597

TITLE: Chimeric proteins containing cytokine receptor binding domain and glycosylphosphatidylinositol anchor and their therapeutic uses

INVENTOR(S): Ross, Richard; Sayers, Jon; Artymiuk, Peter

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004090135	A2	20041021	WO 2004-GB1572	20040407
WO 2004090135	A3	20050428		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,

TD, TG
EP 1616010 A2 20060118 EP 2004-726219 20040407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
JP 2007527695 T 20071004 JP 2006-506114 20040407
US 20060205926 A1 20060914 US 2005-552388 20051007
US 7625998 B2 20091201
PRIORITY APPLN. INFO.: GB 2003-8088 A 20030409
GB 2003-24235 A 20031016
WO 2004-GB1572 W 20040407
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention relates to polypeptides which comprise a ligand-binding domain of a cytokine receptor fused with a signal sequence for the attachment of glycosylphosphatidylinositol (GPI) anchors. GPI-anchors are post-translational modifications to proteins that add glycosylphosphatidylinositol which enable these proteins to anchor to the extracellular side of cell membranes. 1B1-GP1 was constructed, in which GH was linked through its C-terminus to the extracellular domain of the GH receptor and then linked to the GPI signal sequence. 1C1-GPI was also constructed, in which a tandem of GH was linked through the second GH C-terminus to the GPI signal sequence. The invention provides vectors and CHO-K1 cells for expressing GHBP-GPI.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 16 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:225928 BIOSIS
DOCUMENT NUMBER: PREV200400225966
TITLE: Tandem fusions of growth hormone and its G120R mutated antagonist retain biological activity and demonstrate prolonged plasma half-life.
AUTHOR(S): Pradhananga, S. L. [Reprint Author]; Wilkinson, I. [Reprint Author]; Haylor, J. [Reprint Author]; Rezaee, S. [Reprint Author]; Artymiuk, P.; Sayers, J.; Ross, R. J. M. [Reprint Author]
CORPORATE SOURCE: Department of Clinical Sciences, Sheffield University, Sheffield, UK
SOURCE: Growth Hormone & IGF Research, (April 2004) Vol. 14, No. 2, pp. 116. print.
Meeting Info.: Second International GH-IGF Symposium. Queensland, Australia. April 18-22, 2004.
ISSN: 1096-6374 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Apr 2004
Last Updated on STN: 21 Apr 2004

L6 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:591215 CAPLUS
DOCUMENT NUMBER: 139:144956
TITLE: Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in therapy
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062276	A2	20030731	WO 2003-GB253	20030124
WO 2003062276	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2510751	A1	20030731	CA 2003-2510751	20030124
EP 1468020	A2	20041020	EP 2003-702702	20030124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005529583	T	20051006	JP 2003-562153	20030124
RU 2325400	C2	20080527	RU 2004-121969	20030124
MX 2004007160	A	20050331	MX 2004-7160	20040723
BR 2004003173	A	20060321	BR 2004-3173	20040730
US 20050214762	A1	20050929	US 2005-502344	20050511
PRIORITY APPLN. INFO.:			GB 2002-1679 A	20020125
			WO 2003-GB253 W	20030124

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to the provision of oligomeric polypeptides (dimers, trimers, etc) comprising the ligand binding domains of cytokines which are linked via flexible polypeptide linker mols. The linker mols. optionally comprise protease sensitive sites to modulate the release of biol. active cytokines when administered to a human or animal subject. The invention also relates to chemical crosslinkers wherein the chemical crosslinkers serve to link the ligand binding domains. The chimeric cytokine can be used for treating acromegaly, gigantism, GH deficiency, Turners syndrome, renal failure, osteoporosis, diabetes mellitus, cancer, obesity, insulin resistance, hyperlipidemia, hypertension, anemia, autoimmune and infectious disease, inflammatory disorders including rheumatoid arthritis.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:924005 CAPLUS
DOCUMENT NUMBER: 136:49347
TITLE: Chimeric binding agent comprising cytokine, linker and cytokine receptor and uses in modulating receptor activity and therapy
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     --------------      ----   --------    -------------------      --------
     WO 2001096565        A2    20011220    WO 2001-GB2645           20010618
     WO 2001096565        A3    20020801
        W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
            RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
            UZ, VN, YU, ZA, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2447632           A1    20011220    CA 2001-2447632          20010618
     EP 1290170           A2    20030312    EP 2001-940731           20010618
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004503243        T     20040205    JP 2002-510682           20010618
     US 20040071655       A1    20040415    US 2003-311473           20030718
     US 7446183           B2    20081104
     US 20090054336       A1    20090226    US 2008-175582           20080718
PRIORITY APPLN. INFO.:                      GB 2000-14765       A    20000616
                                            GB 2001-5969        A    20010310
                                            GB 2001-6487        A    20010316
                                            WO 2001-GB2645      W    20010618
                                            US 2003-311473      A1   20030718
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB   The invention provides a binding agent comprising a first part capable of
     binding a ligand binding domain of a receptor linked to a second part
     comprising a receptor binding domain wherein said binding agent modulates
     the activity of the receptor.  The inventors link growth
     hormone (GH), through its C-terminal and a linker to the
     N-terminus of the SD100 domain of growth hormone
     receptor (GHR).  By varying the length of the linker inventors define a
     mol. that has the flexibility to allow binding of GH through site 1 to
     full length receptor at the cell surface.  The invention also relates to
     methods, vectors and host cells for production of said chimeric binding agent.
OS.CITING REF COUNT:     6      THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
                                (6 CITINGS)
REFERENCE COUNT:         9      THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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     (FILE 'HOME' ENTERED AT 14:56:38 ON 28 JUN 2010)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:57:00 ON 28 JUN 2010
L1          385 S SAYERS J?/AU
L2           22 S L1 AND GROWTH(W)HORMONE
L3           19 DUP REM L2 (3 DUPLICATES REMOVED)
L4          363 S ARTYMIUK P?/AU
L5           19 S L4 AND GROWTH(W)HORMONE
L6           16 DUP REM L5 (3 DUPLICATES REMOVED)
L7        11282 S ROSS R?/AU
L8          365 S L7 AND GROWTH(W)HORMONE
L9           28 S L8 AND LIGAND
L10          16 DUP REM L9 (12 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:01:53 ON 28 JUN 2010
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FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:09:50 ON 28 JUN 2010

FILE 'STNGUIDE' ENTERED AT 15:09:52 ON 28 JUN 2010

=> dis ibib abs l10 1-16
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y)/N:y

L10 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2009:1048978 CAPLUS
DOCUMENT NUMBER: 151:307229
TITLE: Linker peptides including glycosylation sites for use in fusion proteins
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 185pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009103965	A1	20090827	WO 2009-GB437	20090218
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: GB 2008-2978 A 20080219
GB 2008-21076 A 20081119
GB 2009-539 A 20090114
OTHER SOURCE(S): MARPAT 151:307229
AB Peptide linkers that contain a glycosylation site and that can be used in the manufacture of fusion proteins that interact with membranes, e.g. fusion proteins of proteins and their cognate receptors. Glycosylation site motif variants for use in linker peptides are described.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2009:115655 CAPLUS
DOCUMENT NUMBER: 150:161106
TITLE: Growth hormone fusion proteins
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009013461	A1	20090129	WO 2008-GB2406	20080716
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2008278907	A1	20090129	AU 2008-278907	20080716
CA 2693951	A1	20090129	CA 2008-2693951	20080716
EP 2170943	A1	20100407	EP 2008-775945	20080716
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
KR 2010043201	A	20100428	KR 2010-702192	20080716
CN 101679504	A	20100324	CN 2008-80021473	20091222

PRIORITY APPLN. INFO.:
US 2007-951122P A 20070720
GB 2007-17985 A 20070914
WO 2008-GB2406 W 20080716

AB We disclose growth hormone fusion proteins that have increased in vivo stability and activity; nucleic acid mols. encoding said proteins and methods of treatment of growth hormone deficiency that use said proteins. This disclosure relates to the biol. actions of a ligand-receptor fusion (LR-fusion) of GH with its extracellular domain receptor. Such a genetically engineered LR-fusion protein was purified from mammalian cell culture. In rats the LR-fusion had a 300-times reduced clearance compared to native GH and single administration promoted growth for 10 days far superior to that seen with native GH. The reduced clearance is reproducible in a primate model. The LR-fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone as occurs naturally with GH and its binding protein. A recombinant gene encoding human GH linked to the A & B domains of the GHR extracellular domain (exGHR1-238) via a flexible (Gly4Ser)4 linker, was generated (Fig. 1 c).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2007:1303035 CAPLUS
DOCUMENT NUMBER: 147:535195
TITLE: Fusion protein composed of circularly permuted growth hormone antagonist GHCP07C, extracellular domain of receptor, and human modified prolactin, and its use in construction of pharmaceutical compositions for treating disorders
INVENTOR(S): Pradhananga, Sarbendra; Sayers, John; Ross, Richard; Artymiuk, Peter
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007128979	A1	20071115	WO 2007-GB1285	20070405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007246913	A1	20071115	AU 2007-246913	20070405
CA 2648487	A1	20071115	CA 2007-2648487	20070405
EP 2004681	A1	20081224	EP 2007-732329	20070405
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2009532051	T	20090910	JP 2009-503658	20070405
CN 101389649	A	20090318	CN 2007-80006944	20080827
KR 2008109814	A	20081217	KR 2008-724266	20081002
MX 2008012934	A	20081015	MX 2008-12934	20081006
IN 2008KN04414	A	20090306	IN 2008-KN4414	20081103
US 20100035804	A1	20100211	US 2009-296180	20090616

PRIORITY APPLN. INFO.: GB 2006-6946 A 20060406
WO 2007-GB1285 W 20070405

AB The invention provides nucleic acid mols. encoding the circularly permuted human growth hormone GHCP07 and variants thereof, wherein variants contain amino acid changes at the receptor binding sites and acts as growth hormone receptor antagonists. The invention also provides the amino acid sequences of GHCP07, and antagonist GHCP07C, wherein GHCP07C contains a C-terminal region of human growth hormone (GH) linked to a N-terminal region of GH, with a changes in amino acids at receptor binding sites, such as Glycine to Arginine at position 176. The invention further provides various fusion proteins comprised of: (a) at least two GHCP07C polypeptides linked in tandem; (b) extracellular binding domains of growth hormone receptor (GHR) linked to at least two GHCP07 polypeptides; (c) GHCP07C polypeptides linked to a human prolactin modified polypeptide (such as G129R PRL); and/or (d) GHCP07C-human modified prolactin fusions containing an extracellular domain of receptors, such as cytokine, GH, prolactin receptors. The invention was based on the general knowledge that the G129R mutation in PRL and G120R mutation in GH disrupt the structural integrity of the two receptor sites, and results in proteins acting as receptor antagonists. Still further, the invention provides: (a) nucleic acid mols. encoding the disclosed fusion proteins and their use in construction of vectors for recombinant protein production; and (b) the amino acid sequences of said extracellilar domains found in human GHR and the modified human prolactin (G129R). Finally, the invention provides for the use of the disclosed antagonists, and/or their fusion proteins, and/or their nucleic acids in construction of a pharmaceutical compn which can be use to treat various conditions, such as gigantism, acromegaly, cancer, diabetic retinopathy, diabetic nephropathy and/or other complications of diabetes and/or GH excess. In the examples, the invention presented mol. genetics methods used to generate circularly permutated growth

hormone antagonists GHCP07BHis and GHCP07C, and showed that both proteins had antagonistic activity.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 16 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2007527470 MEDLINE

DOCUMENT NUMBER: PubMed ID: 17721547

TITLE: A ligand-receptor fusion of growth hormone forms a dimer and is a potent long-acting agonist.

AUTHOR: Wilkinson Ian R; Ferrandis Eric; Artymiuk Peter J; Teillot Marc; Soulard Chantal; Touvay Caroline; Pradhananga Sarbendra L; Justice Sue; Wu Zida; Leung Kin C; Strasburger Christian J; Sayers Jon R; Ross Richard J

CORPORATE SOURCE: School of Medicine and Biomedical Sciences, Royal Hallamshire Hospital, University of Sheffield, Sheffield S10 2JF, UK.

SOURCE: Nature medicine, (2007 Sep) Vol. 13, No. 9, pp. 1108-13. Electronic Publication: 2007-08-26. Journal code: 9502015. ISSN: 1078-8956. L-ISSN: 1078-8956.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200803

ENTRY DATE: Entered STN: 11 Sep 2007 Last Updated on STN: 13 Mar 2008 Entered Medline: 12 Mar 2008

AB Cytokine hormones have a short plasma half-life and require frequent administration. For example, growth hormone replacement involves daily injections. In common with other cytokines, the extracellular domain of the growth hormone receptor circulates as a binding protein, which naturally prolongs the biological half-life of growth hormone. Here we have studied the biological actions of a ligand-receptor fusion of growth hormone and the extracellular domain of its receptor. The genetically engineered ligand-receptor fusion protein was purified from mammalian cell culture. In rats, the ligand-receptor fusion had a 300-times reduced clearance as compared to native growth hormone, and a single injection promoted growth for 10 d, far exceeding the growth seen after administration of native growth hormone. The ligand-receptor fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone similar to the natural reservoir of growth hormone and its binding protein. In conclusion, a ligand-receptor fusion of cytokine to its extracellular receptor generates a potent, long-acting agonist with exceptionally slow absorption and elimination. This approach could be easily applied to other cytokines.

L10 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:104499 CAPLUS

DOCUMENT NUMBER: 144:219144

TITLE: Recombinant dimers of cytokine receptor-binding domains linked by inflexible helical linkers for modulation of cytokine signaling

INVENTOR(S): Artymiuk, Peter; Pradhananga, Sarbendra; Sayers, John;

Ross, Richard
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010891	A2	20060202	WO 2005-GB2826	20050718
WO 2006010891	A9	20060427		
WO 2006010891	A3	20060608		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SZ, BE, CY, FR, GR, IE, IT, MC, NL, SI, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005266184	A1	20060202	AU 2005-266184	20050718
CA 2575441	A1	20060202	CA 2005-2575441	20050718
EP 1771467	A2	20070411	EP 2005-761593	20050718
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101014616	A	20070808	CN 2005-80030121	20050718
JP 2008507292	T	20080313	JP 2007-523141	20050718
NZ 553224	A	20090531	NZ 2005-553224	20050718
RU 2391353	C2	20100610	RU 2007-106043	20050718
MX 2007001180	A	20070413	MX 2007-1180	20070126
KR 2007067678	A	20070628	KR 2007-703976	20070220
KR 891509	B1	20090406		
IN 2007KN00631	A	20070706	IN 2007-KN631	20070221
KR 2009006221	A	20090114	KR 2008-729058	20081127
US 20090221477	A1	20090903	US 2009-658526	20090416

PRIORITY APPLN. INFO.:	US 2004-591358P	P	20040726
	GB 2004-16687	A	20040727
	GB 2005-2839	A	20050211
	WO 2005-GB2826	W	20050718
	KR 2007-703976	A3	20070220

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB We disclose therapeutic proteins comprising at least two domains capable of binding to a cytokine receptor, wherein the domains are connected by a peptide linker, wherein the linker optionally comprises a rigid alpha helical region. These proteins may act as agonists or antagonists of cytokine signaling. Thus, growth hormone receptor-binding growth hormone fragments were dimerized using a rigid or semi-rigid linker. The rigid linker comprised the motif A(EAAAK)nA, with n = 1-5 preferred. These proteins were produced with transgenic E. coli. The growth hormone activity of these proteins was equal to or greater than growth hormone itself.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 16 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2006194908 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16464942
TITLE: A mutant signal transducer and activator of transcription 5b, associated with growth hormone insensitivity and insulin-like growth factor-I deficiency, cannot function as a signal transducer or transcription factor.
AUTHOR: Fang Peng; Kofoed Eric M; Little Brian M; Wang Xiangdong; Ross Richard J M; Frank Stuart J; Hwa Vivian; Rosenfeld Ron G
CORPORATE SOURCE: Department of Pediatrics, NRC5, Oregon Health and Science University, 3181 Southwest Sam Jackson Park Road, Portland, OR 97239-3098, USA.
CONTRACT NUMBER: CA 58110 (United States NCI NIH HHS)
DK 46395 (United States NIDDK NIH HHS)
SOURCE: The Journal of clinical endocrinology and metabolism, (2006 Apr) Vol. 91, No. 4, pp. 1526-34. Electronic Publication: 2006-02-07.
Journal code: 0375362. ISSN: 0021-972X. L-ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 8 Apr 2006
Last Updated on STN: 2 May 2006
Entered Medline: 1 May 2006

AB CONTEXT: A natural missense mutation in the signal transducer and activator of transcription (STAT) 5b gene was recently identified in association with a female patient presenting with severe growth failure and immune dysfunction. The mutation results in an alanine to proline substitution at residue 630 (A630P) in the src-homology-2 domain, a region essential for docking of STATs to phospho-tyrosines on activated receptors, STAT dimerization, and stabilization of phospho-STAT-DNA interactions. OBJECTIVE: The purpose of this study was to explore the molecular mechanisms underlying the GH insensitivity and IGF-I deficiency caused by the A630P-mutated STAT5b. RESULTS: In reconstitution experiments using HEK293 cells, both GH and interferon-gamma were unable to activate mutant STAT5b (A630P), as demonstrated by lack of immunodetectable phospho-tyrosyl-STAT5b (A630P) and inability to drive luciferase reporter activity. However, the Src family of nonreceptor kinases [constitutively active v-src and epithelial growth factor-induced c-src] tyrosine-phosphorylated STAT5b(A630P). The v-src-induced phospho-STAT5b(A630P) translocated to the nucleus but, unlike wild-type Stat5b, was unable to bind DNA. CONCLUSIONS: The A630P mutation disrupts the src-homology-2 architecture such that: 1) mutant STAT5b most likely cannot dock to phospho-tyrosines on ligand-activated receptors; and 2) stable interactions with DNA are prevented. Because STAT5b (A630P) is an inefficient signal transducer and transcription factor, the detrimental impact on signaling pathways important for normal growth and immunity explains, in part, the complex clinical phenotype of GH insensitivity and immune dysfunction.

L10 ANSWER 7 OF 16 MEDLINE on STN

ACCESSION NUMBER: 2006076164 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16461551
TITLE: A 36 residues insertion in the dimerization domain of the growth hormone receptor results in defective trafficking rather than impaired signaling.
AUTHOR: Maamra M; Milward A; Esfahani H Zarkesh; Abbott L P; Metherell L A; Savage M O; Clark A J L; Ross R J M
CORPORATE SOURCE: Division of Clinical Sciences (North), University of Sheffield, Clinical Sciences Centre, Northern General Hospital, Sheffield S5 7AU, UK.
SOURCE: The Journal of endocrinology, (2006 Feb) Vol. 188, No. 2, pp. 251-61.
Journal code: 0375363. ISSN: 0022-0795. L-ISSN: 0022-0795.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200604
ENTRY DATE: Entered STN: 8 Feb 2006
Last Updated on STN: 5 Apr 2006
Entered Medline: 4 Apr 2006

AB Growth hormone insensitivity syndrome (GHIS) has been reported in a family homozygous for a point mutation in the GH receptor (GHR) that activates an intronic pseudoexon. The resultant GHR (GHR1-656) includes a 36 amino-acids insertion after residue 207, in the region known to be important for homodimerization of GHR. We have examined the functional consequences of such an insertion in mammalian cells transfected with the wild type (GHRwt) and mutated GHR (GHR1-656). Radio-ligand binding and flow cytometry analysis showed that GHR1-656 is poorly expressed at the cell surface compared with GHRwt. Total membrane binding and Western blot analysis showed no such difference in the level of total cellular GHR expressed for GHR1-656 vs GHRwt. Immunofluorescence showed GHR1-656 to have different cellular distribution to the wild type receptor (GHRwt), with the mutated GHR being mainly perinuclear and less vesicular than GHRwt. Western blot analysis showed GH-induced phosphorylation of Jak2 and Stat5 for both GHR1-656 and GHRwt, although reduced Stat5 activity was detected with GHR1-656, consistent with lower levels of expression of GHR1-656 than GHRwt at the cell surface. In conclusion, we report that GHIS, due to a 36 amino-acids insertion in the extracellular domain of GHR, is likely to be explained by a trafficking defect rather than by a signalling defect of GHR.

L10 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2005:34776 CAPLUS
DOCUMENT NUMBER: 142:127937
TITLE: Modified cytokine ligand polypeptides preparation, screening, and uses thereof for treatment
INVENTOR(S): Sayers, Jon; Artymuik, Peter; Ross, Richard
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003165	A2	20050113	WO 2004-GB2827	20040628
WO 2005003165	A3	20050714		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2568859	A1	20050113	CA 2004-2568859		20040628
EP 1639002	A2	20060329	EP 2004-743175		20040628
EP 1639002	B1	20100505			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

JP 2008504001	T	20080214	JP 2006-518330		20040628
AT 466880	T	20100515	AT 2004-743175		20040628
US 20070264234	A1	20071115	US 2007-561831		20070316
PRIORITY APPLN. INFO.:			GB 2003-15182	A	20030628
			WO 2004-GB2827	W	20040628

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The disclosed invention describes modified cytokine ligand polypeptides comprising a modified amino acid sequence which is a modification of the native cytokine amino acid sequence of said ligand, wherein the native N terminal and C terminal amino acid residues of the native polypeptide are linked, directly or indirectly, together, characterized in that said ligand is provided with alternative N terminal and C terminal amino acid residues and further wherein at least one binding domain for said ligand's cognate binding partner or receptor complex is disrupted. The authors describe the first embodiment of the growth hormone circular permutation GH CP01, with the N terminus Ile121 and the C terminus Glu118. The "old" termini of GH were linked by a 6 amino acid linker, formed by joining the "old" termini -3 amino acids from the first helix at the N terminus and +3 residues for the last helix at the C terminus. E. coli cells were used as the expression system. Also described are alternative approaches to construct circular permutations of GH.

OS.CITING REF COUNT:	2	THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT:	3	THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER:	2004:878488 CAPLUS
DOCUMENT NUMBER:	141:344597
TITLE:	Chimeric proteins containing cytokine receptor binding domain and glycosylphosphatidylinositol anchor and their therapeutic uses
INVENTOR(S):	Ross, Richard; Sayers, Jon; Artymiuk, Peter
PATENT ASSIGNEE(S):	Asterion Limited, UK
SOURCE:	PCT Int. Appl., 40 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004090135	A2	20041021	WO 2004-GB1572	20040407

WO 2004090135 A3 20050428
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1616010 A2 20060118 EP 2004-726219 20040407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
JP 2007527695 T 20071004 JP 2006-506114 20040407
US 20060205926 A1 20060914 US 2005-552388 20051007
US 7625998 B2 20091201
PRIORITY APPLN. INFO.: GB 2003-8088 A 20030409
GB 2003-24235 A 20031016
WO 2004-GB1572 W 20040407

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to polypeptides which comprise a ligand-binding domain of a cytokine receptor fused with a signal sequence for the attachment of glycosylphosphatidylinositol (GPI) anchors. GPI-anchors are post-translational modifications to proteins that add glycosylphosphatidylinositol which enable these proteins to anchor to the extracellular side of cell membranes. 1B1-GP1 was constructed, in which GH was linked through its C-terminus to the extracellular domain of the GH receptor and then linked to the GPI signal sequence. 1C1-GPI was also constructed, in which a tandem of GH was linked through the second GH C-terminus to the GPI signal sequence. The invention provides vectors and CHO-K1 cells for expressing GHBP-GPI.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 16 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004448217 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15356058
TITLE: Pegvisomant, a growth hormone-specific antagonist, undergoes cellular internalization.
AUTHOR: Maamra M; Kopchick J J; Strasburger C J; Ross R J M
CORPORATE SOURCE: Sheffield University, Clinical Sciences, Northern General Hospital, Sheffield, United Kingdom.
SOURCE: The Journal of clinical endocrinology and metabolism, (2004 Sep) Vol. 89, No. 9, pp. 4532-7.
Journal code: 0375362. ISSN: 0021-972X. L-ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 10 Sep 2004
Last Updated on STN: 8 Oct 2004
Entered Medline: 7 Oct 2004

AB GH binding to a receptor (GHR) dimer triggers signaling and internalization of the receptor/ligand complex. Pegvisomant is a specific GH antagonist developed for the treatment of acromegaly, and

the basic molecule is GH with an amino acid substitution that blocks the conformational change necessary to generate functional GHR dimerization required for signal transduction. Pegvisomant has additional polyethylene glycol moieties to prolong its half-life in the circulation and improve clinical efficacy through reduced renal clearance. Pegvisomant has a long plasma half-life, and its mode of clearance has not been established. We have studied pegvisomant internalization and demonstrate that despite its size and prolonged plasma half-life, it is internalized by cells expressing the GHR. As pegvisomant does not activate intracellular signal transduction systems, our results support the concept that the conformational changes required for GHR signaling are not essential for the intracellular trafficking of the ligand and establish one potential contributing mechanism for pegvisomant clearance.

L10 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:591215 CAPLUS
DOCUMENT NUMBER: 139:144956
TITLE: Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in therapy
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062276	A2	20030731	WO 2003-GB253	20030124
WO 2003062276	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2510751	A1	20030731	CA 2003-2510751	20030124
EP 1468020	A2	20041020	EP 2003-702702	20030124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005529583	T	20051006	JP 2003-562153	20030124
RU 2325400	C2	20080527	RU 2004-121969	20030124
MX 2004007160	A	20050331	MX 2004-7160	20040723
BR 2004003173	A	20060321	BR 2004-3173	20040730
US 20050214762	A1	20050929	US 2005-502344	20050511
PRIORITY APPLN. INFO.:			GB 2002-1679 A	20020125
			WO 2003-GB253 W	20030124

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to the provision of oligomeric polypeptides (dimers, trimers, etc) comprising the ligand binding domains of cytokines which are linked via flexible polypeptide linker mols. The linker mols. optionally comprise protease sensitive sites to modulate the release of biol. active cytokines when administered to a human or animal subject. The invention also relates to chemical crosslinkers wherein the chemical

crosslinkers serve to link the ligand binding domains. The chimeric cytokine can be used for treating acromegaly, gigantism, GH deficiency, Turners syndrome, renal failure, osteoporosis, diabetes mellitus, cancer, obesity, insulin resistance, hyperlipidemia, hypertension, anemia, autoimmune and infectious disease, inflammatory disorders including rheumatoid arthritis.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:180984 CAPLUS

DOCUMENT NUMBER: 140:194483

TITLE: Chimeric proteins containing cytokine receptor binding domain and glycosylphosphatidylinositol-containing signaling peptide and their therapeutic uses

INVENTOR(S): Ross, Richard

PATENT ASSIGNEE(S): Asterion Ltd., UK

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003034275	A2	20030424	WO 2002-GB4665	20021011
WO 2003034275	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2380735	A	20030416	GB 2001-24620	20011013
CA 2494706	A1	20030424	CA 2002-2494706	20021011
JP 2005505307	T	20050224	JP 2003-536934	20021011
JP 4384492	B2	20091216		
AU 2002334161	B2	20070329	AU 2002-334161	20021011
RU 2340628	C2	20081210	RU 2004-111007	20021011
EP 1446733	B1	20090909	EP 2002-801405	20021011
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SK, TR				
AT 442444	T	20090915	AT 2002-801405	20021011
HU 2004001611	A3	20100128	HU 2004-1611	20021011
KR 2010039911	A	20100416	KR 2010-707082	20021011
US 20050059577	A1	20050317	US 2004-492403	20040413
US 7485713	B2	20090203		

PRIORITY APPLN. INFO.:

GB 2001-24620	A	20011013
GB 2002-904	A	20020116
GB 2002-18889	A	20020814
KR 2004-705419	A3	20021011
WO 2002-GB4665	W	20021011

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to polypeptides which comprise a

cytokine-binding domain of a cytokine receptor fused with a signal sequence for the attachment of glycosylphosphatidylinositol (GPI) anchors. The cytokine receptor variants lack a cytoplasmic domain and therefore do not have the capability to signal. The provision of a GPI-anchor domain means the variant inserts into membranes and acts as an effective inhibitor of GH signaling by competing for circulating cytokine and binding cytokine at the cell surface in a heterodimeric complex that consists of the chimeric truncated GPI anchored receptor, cytokine, and the native receptor. In addition, truncated GPI-anchored receptor generates a large amount of soluble receptor which will bind its ligand. In a preferred embodiment, the chimeric protein acts as an antagonist following local or transgenic expression through gene therapy. Thus, the cDNA extracellular domain of human growth hormone receptor (bases 98-834 of GenBank X06562) is ligated into a vector (pAc6-LP-MCS-GPI) containing the Dictyostelium actin 6 gene promoter, a Dictyostelium signal peptide coding region, multiple, cloning site, and the signal for a GPI anchor, and the construct is transfected into Dicytostelium cells. To demonstrate that growth hormone receptor-GPI can act as a transgenic therapy, the extracellular domain of the growth hormone receptor is cloned upstream of a human GPI signal sequence into a mammalian expression vector.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:550165 CAPLUS

DOCUMENT NUMBER: 139:112729

TITLE: Chimeric growth hormone-growth hormone receptor proteins and therapeutic uses thereof

INVENTOR(S): Ross, Richard; Sayers, Jon; Artymuik, Peter

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: Brit. UK Pat. Appl., 46 pp.
CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2384001	A	20030716	GB 2001-30052	20011214
GB 2384001	B	20040204		
GB 2389115	A	20031203	GB 2003-20479	20011214
GB 2389115	B	20050316		
CA 2468439	A1	20030828	CA 2002-2468439	20021206
WO 2003070765	A2	20030828	WO 2002-GB5523	20021206
WO 2003070765	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002366325	A1	20030909	AU 2002-366325	20021206

AU	2002366325	B2	20080424			
EP	1456385	A2	20040915	EP	2002-806858	20021206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK						
HU	2004002496	A2	20050329	HU	2004-2496	20021206
CN	1604965	A	20050406	CN	2002-824781	20021206
CN	100558899	C	20091111			
JP	2005525106	T	20050825	JP	2003-569672	20021206
NZ	533550	A	20060224	NZ	2002-533550	20021206
NZ	543369	A	20070831	NZ	2002-543369	20021206
RU	2346047	C2	20090210	RU	2004-117777	20021206
CN	101638437	A	20100203	CN	2009-10164026	20021206
SG	160205	A1	20100429	SG	2007-5155	20021206
IN	2004KN00751	A	20060421	IN	2004-KN751	20040603
IN	227610	A1	20090116			
ZA	2004004488	A	20060329	ZA	2004-4488	20040607
MX	2004005675	A	20050419	MX	2004-5675	20040611
BR	2004003522	A	20060411	BR	2004-3522	20040825
US	20050123558	A1	20050609	US	2005-498497	20050114
US	7524649	B2	20090428			
ZA	2006000149	A	20061025	ZA	2006-149	20060106
KR	2006106862	A	20061012	KR	2006-716929	20060823
KR	848802	B1	20080728			
KR	2007108254	A	20071108	KR	2007-721636	20070920
KR	879553	B1	20090122			
IN	2008KN01333	A	20081226	IN	2008-KN1333	20080402
AU	2008201889	A1	20080522	AU	2008-201889	20080430
US	20090239801	A1	20090924	US	2009-389022	20090219
JP	2010043100	A	20100225	JP	2009-223065	20090928

PRIORITY APPLN. INFO.:	GB 2001-30052	A3	20011214
	AU 2002-366325	A3	20021206
	CN 2002-824781	A3	20021206
	JP 2003-569672	A3	20021206
	NZ 2002-533550	A3	20021206
	WO 2002-GB5523	W	20021206
	IN 2004-KN751	A3	20040603
	KR 2004-709055	A3	20040611
	US 2005-498497	A3	20050114
	KR 2006-716929	A3	20060823

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A chimeric polypeptide comprising at least one modified binding domain of growth hormone (GH) and a ligand binding domain of growth hormone receptor (GHR) is claimed, wherein the modification is the addition, deletion or substitution of at least one amino acid. Said binding domain may be site 1 of growth hormone, site 2 of growth hormone or both sites of growth hormone. The binding domain of the growth hormone receptor may be the extracellular domain of GHR more preferably the C-terminal SD-100 domain. Nucleic acids encoding such polypeptides, expression vectors and cells expressing such vectors are also claimed. The use of such polypeptides in the preparation of pharmaceuticals and in the treatment of diseases including gigantism, acromegaly, cancer and diabetic conditions is also claimed. Alternatively claimed is a chimeric polypeptide comprising more than two modified growth hormone binding domains.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:300688 CAPLUS
DOCUMENT NUMBER: 138:315840

TITLE: Preparation of GPI-anchored proteins with cytokine receptor ligand binding domain and signal sequence
INVENTOR(S): Ross, Richard
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: Brit. UK Pat. Appl., 41 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2380735	A	20030416	GB 2001-24620	20011013
CA 2494706	A1	20030424	CA 2002-2494706	20021011
WO 2003034275	A2	20030424	WO 2002-GB4665	20021011
WO 2003034275	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1568330	A	20050119	CN 2002-820277	20021011
JP 2005505307	T	20050224	JP 2003-536934	20021011
JP 4384492	B2	20091216		
AU 2002334161	B2	20070329	AU 2002-334161	20021011
RU 2340628	C2	20081210	RU 2004-111007	20021011
EP 1446733	B1	20090909	EP 2002-801405	20021011
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SK, TR				
AT 442444	T	20090915	AT 2002-801405	20021011
PT 1446733	E	20090928	PT 2002-801405	20021011
ES 2329228	T3	20091124	ES 2002-801405	20021011
HU 2004001611	A3	20100128	HU 2004-1611	20021011
KR 2010039911	A	20100416	KR 2010-707082	20021011
US 20050059577	A1	20050317	US 2004-492403	20040413
US 7485713	B2	20090203		

PRIORITY APPLN. INFO.:

GB 2001-24620	A	20011013
GB 2002-904	A	20020116
GB 2002-18889	A	20020814
KR 2004-705419	A3	20021011
WO 2002-GB4665	W	20021011

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to polypeptides which comprise a receptor binding domain of a cytokine and a domain which includes a signal sequence for the attachment of glycosylphosphhatidylinositol (GPI) anchors. The invention also relates to methods to manufacture the polypeptides, nucleic acids, mols. encoding the polypeptides and therapeutic compns. by comprising the polypeptides.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:924005 CAPLUS
DOCUMENT NUMBER: 136:49347

TITLE: Chimeric binding agent comprising cytokine, linker and cytokine receptor and uses in modulating receptor activity and therapy
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096565	A2	20011220	WO 2001-GB2645	20010618
WO 2001096565	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2447632	A1	20011220	CA 2001-2447632	20010618
EP 1290170	A2	20030312	EP 2001-940731	20010618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004503243	T	20040205	JP 2002-510682	20010618
US 20040071655	A1	20040415	US 2003-311473	20030718
US 7446183	B2	20081104		
US 20090054336	A1	20090226	US 2008-175582	20080718

PRIORITY APPLN. INFO.:

GB 2000-14765	A	20000616
GB 2001-5969	A	20010310
GB 2001-6487	A	20010316
WO 2001-GB2645	W	20010618
US 2003-311473	A1	20030718

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides a binding agent comprising a first part capable of binding a ligand binding domain of a receptor linked to a second part comprising a receptor binding domain wherein said binding agent modulates the activity of the receptor. The inventors link growth hormone (GH), through its C-terminal and a linker to the N-terminus of the SD100 domain of growth hormone receptor (GHR). By varying the length of the linker inventors define a mol. that has the flexibility to allow binding of GH through site 1 to full length receptor at the cell surface. The invention also relates to methods, vectors and host cells for production of said chimeric binding agent.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 16 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1999262630 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10329677
TITLE: Studies with a growth hormone antagonist and dual-fluorescent confocal microscopy demonstrate that the full-length human growth hormone receptor, but not the truncated isoform, is

very rapidly internalized independent of Jak2-Stat5 signaling.

AUTHOR: Maamra M; Finidori J; Von Laue S; Simon S; Justice S; Webster J; Dower S; Ross R

CORPORATE SOURCE: Divisions of Clinical Sciences, Sheffield University, Sheffield S5 7AU, United Kingdom.

SOURCE: The Journal of biological chemistry, (1999 May 21) Vol. 274, No. 21, pp. 14791-8.
Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199907

ENTRY DATE: Entered STN: 27 Jul 1999
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AB We have investigated trafficking of two negative regulators of growth hormone receptor (GHR) signaling: a human, truncated receptor, GHR1-279, and a GH antagonist, B2036. Fluorescent-labeled growth hormone (GH) was rapidly internalized by the full-length GHR, with >80% of the hormone internalized within 5 min of exposure to GH. In contrast, <5% of labeled GH was internalized by cells expressing truncated GHR1-279. Using another truncated receptor, GHR1-317 fused to enhanced green fluorescent protein (EGFP), we have exploited fluorescence energy transfer to monitor the trafficking of ligand-receptor complexes. The data confirmed that internalization of this truncated receptor is very inefficient. It was possible to visualize the truncated GHR1-317-EGFP packaged in the endoplasmic reticulum, its rapid movement in membrane bound vesicles to the Golgi apparatus, and subsequent transport to the cell membrane. The GH antagonist, B2036, blocked Jak2-Stat5-mediated GHR signaling but was internalized with a similar time course to native GH. The results: 1) demonstrate the rapid internalization of GH when studied under physiological conditions; 2) confirm the hypothesis that internalization of cytoplasmic domain truncated human GHRs is very inefficient, which explains their dominant negative action; and 3) show that the antagonist action of B2036 is independent of receptor internalization.

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